
Development of novel synNotch CART cell therapy in patients with recurrent EGFRvIII+ glioblastoma

Grant Award Details

Development of novel synNotch CART cell therapy in patients with recurrent EGFRvIII+ glioblastoma

Grant Type: Therapeutic Translational Research Projects

Grant Number: TRAN1-12245

Investigator:

Name:	Hideho Okada
Institution:	University of California, San Francisco
Type:	PI

Disease Focus: Brain Cancer, Cancer, Solid Tumors

Human Stem Cell Use: Somatic Cell

Award Value: \$2,663,144

Status: Pre-Active

Grant Application Details

Application Title: Development of novel synNotch CART cell therapy in patients with recurrent EGFRvIII+ glioblastoma

Public Abstract:**Translational Candidate**

Human T cells transduced with a lentiviral vector encoding anti-EGFRvIII synNotch-primed anti-EphA2/IL-13R α 2 chimeric antigen receptor.

Area of Impact

Glioblastoma is the most common malignant brain tumor, affecting approximately 3 out of 100,000 people/year in the USA with extremely poor prognosis.

Mechanism of Action

In our proposed system, the first antigen EGFRvIII, which is expressed exclusively but heterogeneously on glioblastoma cells, primes the T cells to induce expression of a CAR that recognizes EphA2 and IL-13R α 2, thereby eradicating glioblastoma cells expressing either EphA2 or IL-13R α 2. Efficacy was long-lasting and superior to conventional CART cells. The superb efficacy of these synNotch-CART cells was associated with excellent persistence (>100 days in vivo) and T stem memory cell phenotype.

Unmet Medical Need

Glioblastoma is the most common malignant primary brain tumor, affecting approximately 3 out of 100,000 individuals/year in the USA. Despite surgical resection, radiation and chemotherapy, prognosis remains poor with a 100% recurrence rate and median overall survival of approximately 20 months.

Project Objective

Successful submission of a Pre-IND application

Major Proposed Activities

- Process development for manufacturing of EGFRvIII-primed EphA2/IL-13R α 2 CART cells
- In vivo (rodent) studies to determine preclinical efficacy and safety of the proposed cell products
- Development of the clinical trial protocol, consent form and clinical standard operating procedures (SOPs)

Statement of Benefit to California:

Because the current California's population is nearly 40 million, approximately 1,200 people are likely to be diagnosed with this devastating disease every year. The Brain Tumor Center within the Department of Neurosurgery at UCSF is one of the most established brain tumor research and treatment centers in the world. Our scientists and health care clinicians work in partnership to translate laboratory findings into new or improved forms of clinical therapy for patients in California.

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